PREPARATIONS USED IN THE COLLABORATIVE STUDY

Preparation	Subtype	HBeAg/anti-HBe	Serum/plasma	State
80/549*	*ad*	anti-HBe	Serum	Freeze dried
A	*ad*	HBeAg	Serum	Liquid
B	*ad*	anti-HBe	Plasma	Liquid
C	*ay*	HBeAg	Serum	Liquid
D	*ay*	anti-HBe	Serum	Liquid
E	*ay*	HBeAg	Serum	Liquid
F	*ad*	HBeAg	Serum	Liquid
G†	*ad*	anti-HBe	Serum	Freeze dried

*Proposed British Reference Preparation of Hepatitis B Surface Antigen.
†Coded duplicate of British Reference Preparation

Twelve laboratories contributed data from a total of 31 assays. All participants used solid phase radioimmunoassays—the 'AUSRIA II' commercial kit (Abbott) in six, a modification of the commercial kit in two,[7] and the remaining four laboratories used their local method.

Assay data were analysed using the standard method of parallel line assays;[8] potencies of the samples were expressed relative to the proposed standard. For each sample, potency ratios from replicate assays of individual laboratories were combined by taking their geometric means. The frequency distributions of these values are shown in the figure.

No obvious difference were found between estimates obtained from laboratories using different forms of radioimmunoassay. There was reasonable agreement between the potency estimates obtained by the different laboratories. The potency estimates obtained for the coded duplicate of the standard (sample G) were remarkably close to unity. Furthermore, there was better agreement between laboratories for the potency of sample G than for the other samples. Nevertheless, the variation found between potency estimates of the individual coded preparations for the different laboratories were considered to be small in practical terms.

In 1982 the National Biological Standards Board authorised the establishment of the preparation coded 80/549 as the British Reference Preparation of Hepatitis B Surface Antigen (HsAg), with an assigned unitage of 100 units per ampoule.

The Hepatitis Advisory Group has recommended[9] that all donations of blood destined to contribute to protein fractionation at N.H.S. fractionation centres should be tested by techniques that give a "positive" result for a concentration of 2 British units of HBsAg/ml. Subsequently a further study was carried out to estimate the detection limits, relative to the British Reference Preparation, of methods used by the participants. Preliminary results have shown that laboratories in the study detected the presence of hepatitis antigen at a concentration of 0·5 units/ml. In some laboratories as little as 0·125 units/ml could be routinely detected. Thus the assay methods used in the study should easily fulfil the recommendation of the Hepatitis Advisory Group.

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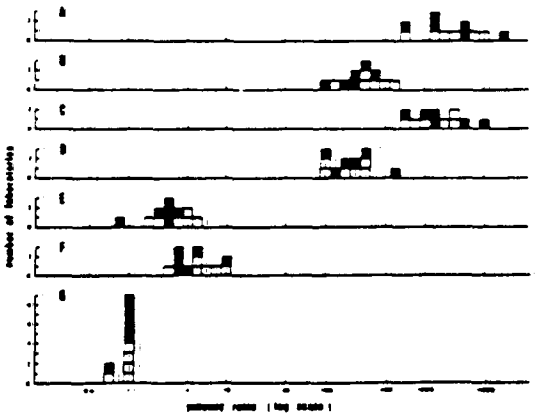

Frequency distributions of potency estimates for samples A–G in terms of proposed reference preparation.

Each box denotes the mean potency obtained by one laboratory by radioimmunoassay: open boxes (Abbott commercial kit), hatched boxes (modification of Abbott kit), filled boxes (other methods).

PASSIVE SMOKING SEVERELY DECREASES PLATELET SENSITIVITY TO ANTIAGGREGATORY PROSTAGLANDINS

SIR,—In the editorial (March 6, p. 548) and in the ensuing correspondence on passive smoking the risk of the development of atherosclerosis has not been mentioned. Unpublished studies (H. S. and O. Burghuber; and E. Walter) suggest that platelet function is severely affected in smokers, and there is some evidence that cigarette smoking might exert its action via diminished vascular prostacyclin (PGI_2) synthesis[1] and decreased sensitivity of platelets to antiaggregatory prostaglandins.[2] We have looked at the effects of passive smoking on platelet sensitivity.

We measured platelet sensitivity to the antiaggregatory prostaglandins (E_1, I_2, D_2) before, during, and after passive smoking in eight male and four female smokers aged 22–31 and in eight male and one female non-smokers aged 24–30. In a 18 m^3 room thirty cigarettes of a strong brand ('Gitanes') were smoked by testers, to give a smoke concentration calculated to resemble that in discos, restaurants, and the like. The test subjects were exposed to the smoke for 15 min. Blood was sampled immediately before and at the end of the smoking period and 20 and 60 min afterwards from a cubital vein without occlusion, with 3·8% sodium citrate as anticoagulant.[3] Platelet sensitivity as expressed as ID_{50} (the amount of PG in ng/ml platelet rich plasma necessary to halve the aggregation induced by 1 μmol/l ADP).

Passive smoking (table) reduced platelet sensitivity to the antiaggregatory PGs, being much more severe in non-smokers than in smokers. 20 min after passive smoking, platelet sensitivity started to return to basal values and this happened more quickly in non-smokers. However, the baseline values in smokers were significantly lower ($p<0·01$) than those in non-smokers.

A decrease in platelet sensitivity is the major determinant of haemostatic regulation[4] and may thus be responsible for early changes preceding atherosclerosis.[5] In combination with our

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PLATELET SENSITIVITY BEFORE AND AFTER PASSIVE SMOKING

PG	Before	End	20 min	60 min
Non-smokers				
I_2	1·26±0·11	2·16±0·21*	1·76±0·21*	1·35±0·19
E_2	18·7±3·1	32·5±4·2*	28·2±4·1*	24·7±2·8
D_2	42·7±3·8	55·6±5·3	51·3±4·2	44·6±4·1
Smokers				
I_2	1·75±0·26	2·08±0·19	2·06±0·15	1·93±0·23
E_2	27·8±2·3	30·6±3·5	31·0±4·1	29·1±2·9
D_2	44·9±4·1	48·6±4·8	49·8±3·7	45·2±3·8

Results in ng PG/ml platelet rich plasma. Mean±SEM.
*$p<0·01$.

findings of decreased PGI_2 formation in umbilical arteries in babies born to mothers who smoked[6] the severe changes we found after passive smoking, especially in non-smokers, point to an important risk in non-smokers exposed to cigarette smoke for a long time. Although not much is known about the long-term influence of passive smoking on the risk for development of atherosclerosis, our data do indicate that passive cigarette smoking, besides being an important social issue, may be a health problem too.

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EARLY TREATMENT OF OESOPHAGEAL VARICES

SIR,—While we agree with Freeman and colleagues (July 10, p. 66) that vasopressin or its analogues may have a place in the management of acute variceal bleeding, we believe its role is at best subsidiary. Since the patients most at risk are those who rebleed early, the aim of management in variceal bleeding should be to prevent rebleeding as much as to control the presenting haemorrhage. To this end we have developed a practice of managing variceal bleeding which provides results equally as good as those obtained with glypressin by Freeman et al. and which also serves as a basis for long-term management.

If bleeding is active, a Linton tube[1] is inflated in the gastric fundus and maintained on traction. When resuscitation is effected the varices are immediately injected with sclerosant with the tube in situ. As there is no oesophageal balloon on this tube, injection is not technically difficult and there is the advantage that a bloodless field is obtained. Furthermore, it seems likely that pressure on the gastric varices aids sclerosis by preventing retrograde flow of sclerosant. If there is no active bleeding at the time of endoscopy the varices are injected without the tube, which can be passed later if bleeding becomes a difficulty. Sclerosis is continued fortnightly until variceal obliteration is complete.

Since adopting this policy 18 months ago we have treated sixteen patients with acute variceal bleeding. One died immediately on admission to hospital before endoscopy could be carried out. Of the remainder, eight had sclerotherapy with the Linton tube in situ and seven had it without the tube. Of these patients, one rebled three times before dying of liver failure due to hepatic angiosarcoma; the other fourteen remain well, although two rebled before their varices were obliterated.

While glypressin might be of value in variceal bleeding when endoscopic sclerotherapy is unavailable, we believe that our simple policy may be of greater value in most general hospitals.

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ICOSAPENTAENOIC ACID AND ISCHAEMIC HEART DISEASE

SIR,—Dr Jones and Dr Davies (July 24, p. 221) discuss the decrease in circulating platelets which various workers have found to be produced by fish oils. But they state that Hay and colleagues[1] used "a similar fish oil and EPA supplement" to that used by Thorngren and Gustafson.[2] There was a crucial difference. Hay et al. used "Maxepa" (Marfleet Refining Company, a subsidiary of Imperial Foods), which is a refined deodorised blend of marine body oils with added antioxidants; it contains about 20% of fatty acids as timnodonic (C20:5$n-3$ or "EPA"), about 19% as clupanodonic (C22:6$n-3$) and less than 1% as cetoleic (C22:1$n-11$). The first two are essential fatty acids and the third is toxic, at least to lower animals, being an isomer of erucic acid (C22:1$n-9$) found in certain rapeseed oils, which cannot be oxidised with ease by muscle mitochondria unless adaptation has occurred and therefore causes myocardial fibrosis with sudden death. Thorngren's volunteers, however, changed their usual Swedish diet for eleven weeks to include "a predominance of fish, mainly mackerel and salmon". These fish have cetoleic acid as a predominant fatty acid, analyses (in % of total acids) by Dr Mary Gale in our Institute being:

Oil	*C20:5*	*C22:6*	*C22:1*
Mackerel (*Scomber scombrus*)	12·1	11·4	9·0
Salmon (*Salmo salar*)	10·2	11·4	11·3

The relevance of C22:1 fatty acids is that they probably decrease the number of circulating platelets. McDonald and colleagues[3] fed seven healthy males for 22 days with rapeseed oil containing 39% erucic acid (which supplied 38% total dietary energy); in five of them there was a marked fall in platelet count which returned to normal when their customary diet was resumed. On a traditional Eskimo diet for 100 days (only seal, fish, and water) my platelet count decreased from 226 000/μl to 52 000/μl, and platelets changed morphologically to giant forms; this diet was very high in C20:5, C22:6, and C22:1. The first of these tended to displace arachidonic acid (C20:4$n-6$) in, for instance, the different phospholipids of platelets[4] and cetoleic acid appeared in these as well as in lipoproteins, erythrocyte membranes, adipose tissue, and skeletal muscle. But the dramatic increase in bleeding time was probably caused partly by the alteration in the structure and therefore fluidity of the platelet membranes and not only by the observed alterations in prostanoids;[5] the former may also have contributed to the decrease in platelet count since Hay et al.[1] observed a decrease on a diet containing negligible cetoleic acid.

The references in Jones and Davies' letter raise an important question of nomenclature. They twice refer to timnodonic acid (C20:5$n-3$) as "eicosopentanoic". This word contains three errors—one academic, one careless (the second "o" should be "a"), and one fundamental. The I.U.P.A.C.-I.U.B. Commission on Biochemical Nomenclature has decreed[6] in its wisdom (or folly) that the Greek εἴκοσι (or the common Epic dialect form ἐείκοσι) must be anglicised as "icosa-" thereby dropping one or two epsilons: so "EPA" must be "IPA". To be on the right side, Professor Crawford and colleagues[7] from the Royal College of Surgeons in a current paper use both spellings in different places. But trivial names for fatty acids are useful; let us continue to call C20:5$n-3$ timnodonic acid and C22:6$n-3$ clupanodonic acid.

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